Population-based incidence and survival of lymphoid neoplasms according to the WHO 2008 classification: Girona (1996-2015)

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INTRODUCTION & OBJECTIVES

• Changing classifications hamper international comparisons of lymphoid neoplasms (LNs) data.

•The aim of this study was to present incidence and survival of LNs in the Girona province (1996-2015) according to the WHO 2008 classification, and to predict the number of LNs in Spain during 2020.

METHODS

• Data were extracted from the population-based Girona cancer registry.

• Incident cases were classified using the ICD-O-3 first revision and grouped according to the WHO 2008 classification scheme.

• Age-adjusted incidence rates (ASR_{E13}) were obtained with Regstattools (1) and incidence trends were modeled using Joinpoint (2).

• Observed and relative survival were estimated with Kaplan-Meier and Ederer II methods, respectively, using WebSurvCa (3).

Table 1. Lymphoid neoplasms incidence rates by subtype. Girona province, 1996-2015.

Subtype	ICD-O-3 codes	N	%	Annual N	Median age (years)	CR	ASR_{E13} (CI 95%)	Sex ratio[1]
Lymphoid neoplasm, total		**4367**	**100.00**	**218**	**67.6**	**33.42**	**37.08 (35.98; 38.21)**	**1.54**
1) Hodgkin lymphoma (HL)		**364**	**8.34**	**18**	**39.7**	**2.79**	**2.72 (2.44; 3.02)**	**1.59**
1.1 Classical Hodgkin lymphoma		336	92.31	17	39.1	2.57	2.5 (2.24; 2.79)	1.55
1.1.1 Lymphocyte rich classical Hodgkin lymphoma	9651	21	6.25	1	34.4	0.16	0.15 (0.09; 0.23)	6.25
1.1.2 Nodular sclerosis classical Hodgkin lymphoma	9663-9667	214	63.69	11	36.7	1.64	1.56 (1.36; 1.79)	1.13
1.1.3 Mixed cellularity classical Hodgkin lymphoma	9652	66	19.64	3	46.4	0.51	0.51 (0.39; 0.65)	2.57
1.1.4 Lymphocyte-depleted classical Hodgkin lymphoma	9653-9655	5	1.49	0	52.5	0.04	0.04 (0.01; 0.09)	NA
1.1.5 Classical Hodgkin lymphoma, NOS	9650,9661-9662	30	8.93	2	53.3	0.23	0.24 (0.16; 0.35)	2.06
1.2 Nodular lymphocyte predominant Hodgkin lymphoma	9659	28	7.69	1	43.8	0.21	0.22 (0.15; 0.32)	2.07
Non-Hodgkin lymphoma (NHL)		**3886**	**88.99**	**194**	**68.6**	**29.74**	**33.35 (32.3; 34.42)**	**1.54**
2) Precursor lymphoid neoplasms		**210**	**4.81**	**10**	**25**	**1.61**	**1.64 (1.42; 1.88)**	**1.53**
2.1 B-lymphoblastic leukemia/lymphoma	9728, 9811-9818, 9836	138	65.71	7	18.2	1.06	1.08 (0.91; 1.28)	1.25
2.2 T-lymphoblastic leukemia/lymphoma	9729, 9837	46	21.90	2	20	0.35	0.34 (0.25; 0.46)	3.53
2.3 Lymphoblastic leukemia/lymphoma, NOS	9727, 9835	26	12.38	1	80	0.2	0.22 (0.14; 0.32)	1.37
3) Mature B-cell neoplasms		**3413**	**78.15**	**171**	**69.7**	**26.12**	**29.5 (28.51; 30.51)**	**1.48**
3.1 Chronic lymphocytic leukemia/small lymphocytic lymphoma	9670, 9823	751	22.00	38	72.4	5.75	6.62 (6.15; 7.11)	1.77
3.2 B-cell prolymphocytic leukemia	9833	-	-	-	-	-	-	-
3.3 Mantle cell lymphoma	9673	105	3.08	5	68.1	0.8	0.92 (0.75; 1.12)	4.37
3.4 Lymphoplasmacytic lymphoma/Macroglobulinemia de Waldenström	9671, 9761	128	3.75	6	73.5	0.98	1.13 (0.94; 1.34)	2.16
3.5 Diffuse large B-cell lymphoma	9678-9680,9688, 9684, 9712, 9735, 9737,9738	733	21.48	37	66.3	5.61	6.18 (5.74; 6.65)	1.4
3.6 Burkitt lymphoma/leukemia	9687, 9826	60	1.76	3	37.9	0.46	0.47 (0.36; 0.61)	1.91
3.7 Marginal lymphoma		339	9.93	17	68.7	2.59	2.92 (2.62; 3.25)	1.09
3.7.1 Splenic marginal zone lymphoma	9689	67	19.76	3	69.2	0.51	0.58 (0.45; 0.74)	1.46
3.7.2 Extranodal marginal zone lymphoma	9699 (excluding C77.0-C77.9)	243	71.68	12	68	1.86	2.09 (1.83; 2.37)	1.07
3.7.3 Nodal marginal zone lymphoma	9699 (C77.0-C77.9)	29	8.55	1	75.8	0.22	0.25 (0.17; 0.36)	0.6
3.8 Follicular lymphoma	9597, 9690, 9691, 9695, 9698	441	12.92	22	62.1	3.37	3.74 (3.4; 4.11)	1.07
3.9 Hairy cell leukemia	9940	32	0.94	2	58.8	0.24	0.26 (0.18; 0.37)	6.86
3.10 Plasma cell neoplasms		820	24.03	41	72.7	6.27	7.22 (6.73; 7.73)	1.41
3.10.1 Solitary plasmocytoma of bone	9731	36	4.39	2	69	0.28	0.31 (0.22; 0.43)	2.1
3.10.2 Extraosseus plasmocytoma	9734	13	1.59	1	76.9	0.1	0.12 (0.07; 0.2)	2.25
3.10.3 Plasma cell myeloma/leukemia	9732-9733	771	94.02	39	72.8	5.9	6.79 (6.32; 7.29)	1.38
3.11 Heavy chain disease	9762	-	-	-	-	-	-	-
3. 12 B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical HL	9596	4	0.12	0	44.5	0.03	0.03 (0.01; 0.08)	1.33
4) Mature-T-cell and NK-cell neoplasms		**263**	**6.02**	**13**	**64.7**	**2.01**	**2.22 (1.96; 2.51)**	**2.59**
4.1 Mycosis fungoides/Sezary syndrome	9700, 9701	81	30.80	4	64.2	0.62	0.69 (0.55; 0.86)	2.78
4.2 Peripheral T/NK-cell lymphoma		130	49.43	6	60.50	0.99	1.08 (0.91; 1.30)	2.95
4.2.1 Peripheral T-cell lymphoma, NOS	9702	60	46.15	3	64.2	0.46	0.5 (0.38; 0.65)	2.52
4.2.2 Angioimmunoblastic T-cell lymphoma	9705	29	22.31	1	70.6	0.22	0.26 (0.17; 0.37)	3.23
4.2.3 Subcutaneous panniculitis-like T-cell lymphoma	9708	2	1.54	0	42	0.02	0.01 (0; 0.05)	0
4.2.4 Anaplastic large cell lymphoma, ALK-positive	9714	18	13.85	1	37	0.14	0.14 (0.08; 0.22)	8.33
4.2.5 Hepatosplenic T-cell lymphoma	9716	3	2.31	0	42.5	0.02	0.02 (0; 0.07)	NA
4.2.6 Enteropathy-associated T-cell lymphoma	9717	1	0.77	0	62.5	0.01	0.01 (0; 0.05)	0
4.2.7 Primary cutaneous gamma-delta T-cell lymphoma	9726	-	-	-	-	-	-	-
4.2.8 Primary cutaneous T-cell lymphoma, NOS	9709	16	12.31	1	73	0.12	0.13 (0.07; 0.22)	3.14
4.2.9 Systemic EBV-positive T-cell lymphoproliferative disease of childhood	9724	-	-	-	-	-	-	-
4.2.10 Hydroa vacciniforme-like lymphoma	9725	1	0.77	0	17.5	0.01	0.01 (0; 0.05)	NA
4.3 Adult T-cell leukemia/lymphoma	9827	3	1.14	0	82.5	0.02	0.02 (0; 0.07)	0.67
4.4 Extranodal NK/Tcell lymphoma, nasal type	9719	11	4.18	1	66.2	0.08	0.09 (0.04; 0.17)	1.86
4.5 T-cell large granular lymphocytic leukemia	9831	22	8.37	1	65	0.17	0.19 (0.12; 0.29)	2.25
4.6 T-cell prolymphocytic leukemia	9834	3	1.14	0	62.5	0.02	0.03 (0.01; 0.08)	0
4.7 Aggressive NK cell leukemia	9948	1	0.38	0	22.5	0.01	0.01 (0; 0.05)	NA
4.8 Primary cutaneous CD30 + T-cell lymphoproliferative disorders	9718	12	4.56	1	70	0.09	0.1 (0.05; 0.18)	2.33
5) Lymphoid neoplasms, NOS	**9590, 9591, 9820, 9970, 9971**	**117**	**2.68**	**6**	**77.9**	**0.9**	**1.01 (0.83; 1.21)**	**1.42**

N, total cases; CR, crude rate; ASR_{E13}, age-standardized incidence rate using European 2013 standard population; CI, confidence interval; [1]Sex ratio (M/F) based on ASR_{E13}; NOS, NOS, no otherwise specified.

Incidence trends (1996 – 2015)

- No statistically significant variations in incidence trends were found for LNs [annual percentage change (APC): 0 (95% CI: -0.8; 0.7)], nor for broader lymphoma categories.
- Incidence trends only increased for peripheral T/NK-cell lymphoma (APC: 4.1 (0.1; 8.3)) and decreased for LNs NOS (APC: -7.4 (-11.2; -3.3)).

Projections (Spain, 2020)

- 17,950 new cases of LNs will be diagnosed in Spain in 2020, of which 1,263 cases will be Hodgkin lymphoma, 738 precursor LNs, 14,360 mature B-cell neoplasms lymphoma, 1,067 mature T-cell and NK-cell neoplasms and 521 LNs NOS.

Table 2. 5-years observed and relative survival of lymphoid neoplasms cases by subtype and sex . Girona province, 1996-2015.

	OS CI (95%)	RS CI (95%)
Hodgkin lymphoma (HL)	**74 (68; 78)**	**76 (71; 81)**
Men	**71 (65; 78)**	**74 (68; 81)**
Women	**77 (70; 84)**	**78 (71; 86)**
Classic HL	72 (67; 77)	75 (70; 80)
Men	70 (63; 77)	72 (66; 80)
Women	76 (69; 84)	77 (70; 86)
Nodular HL	89 (76; 100)	91 (79; 100)
Men	90 (73; 100)	92 (76; 100)
Women	89 (67; 100)	90 (68; 100)
Non-Hodgkin lymphoma	**54 (52; 56)**	**62 (60; 64)**
Men	**52 (50; 55)**	**61 (59; 64)**
Women	**56 (54; 59)**	**62 (60; 65)**
Precursor lymphoid neoplasms	**46 (40; 54)**	**47 (40; 54)**
Men	**46 (38; 56)**	**46 (38; 56)**
Women	**47 (38; 60)**	**48 (38; 60)**
B-lymphoblastic leukemia/lymphoma	54 (46; 63)	54 (46; 63)
Men	55 (46; 68)	55 (45; 68)
Women	55 (45; 68)	55 (45; 68)
T-lymphoblastic leukemia/lymphoma	45 (32; 63)	-
Men	58 (34; 100)	-
Women	42 (28; 63)	-
Lymphoblastic leukemia/lymphoma, NOS	5 (1; 34)	-
Mature B-cell neoplasms	**54 (52; 56)**	**62 (60; 64)**
Men	**52 (50; 55)**	**62 (59; 65)**
Women	**56 (54; 59)**	**63 (60; 66)**
CLL/SLL	65 (62; 69)	80 (76; 85)
Men	65 (61; 70)	82 (76; 88)
Women	66 (61; 72)	78 (71; 85)
Mantle cell lymphoma	44 (35; 56)	51 (40; 65)
Men	47 (37; 61)	55 (43; 70)
Women	11 (2; 62)	-
Lymphoplasmacytic lymphoma/MW	56 (47; 67)	67 (56; 79)
Men	53 (42; 66.7)	65 (52; 82)
Women	61 (47; 79)	-
Diffuse large B-cell lymphoma	46 (42; 50)	50 (46; 54)
Men	45 (40; 50)	50 (45; 56)
Women	47 (41; 53)	50 (44; 56)
Burkitt lymphoma/leukemia	50 (38; 64)	50 (39; 64)
Men	57 (44; 75)	-
Women	55 (25; 86)	56 (25; 87)
Marginal lymphoma	72 (67; 77)	82 (76; 88)
Men	68 (61; 76)	80 (71; 89)
Women	76 (70; 83)	84 (77; 92)
Follicular lymphoma	70 (65; 75)	75 (71; 81)
Men	67 (61; 75)	73 (66; 81)
Women	72 (66; 79)	77 (71; 85)
Hairy cell leukemia	81 (65; 97)	92 (81; 100)
Men	78 (60; 97)	90 (76; 100)
Women	100 (100; 100)	100 (100; 105)
Plasma cell neoplasms	40 (33; 40)	42 (38; 46)
Men	33 (28; 38)	39 (34; 46)
Women	40 (35; 45)	44 (39; 51)
B-cell lymphoma, unclassifiable	75 (26; 100)	75 (26; 100)
Mature-T-cell and NK-cell neoplasms	**57 (51; 64)**	**66 (59; 73)**
Men	**56 (49; 64)**	**65 (57; 74)**
Women	**61 (51; 74)**	**67 (56; 81)**
Mycosis fungoides/Sezary syndrome	79 (71; 89)	90 (80; 100)
Men	81 (69; 93)	92 (84; 100)
Women	76 (52; 99)	85 (66; 100)
Peripheral T/NK-cell lymphoma	38 (30; 48)	43 (34; 54)
Men	34 (25; 45)	39 (29; 53)
Women	50 (23; 77)	52 (25; 79)
Lymphoid neoplasms, NOS	**21 (15; 32)**	**28 (19; 41)**
Men	**20 (11; 35)**	**-**
Women	**23 (14; 40)**	**-**

N, total cases; OS, observed survival; CI, confidence interval; RS, relative survival; NOS, no otherwise specified; DCO cases were excluded from the survival analyses.

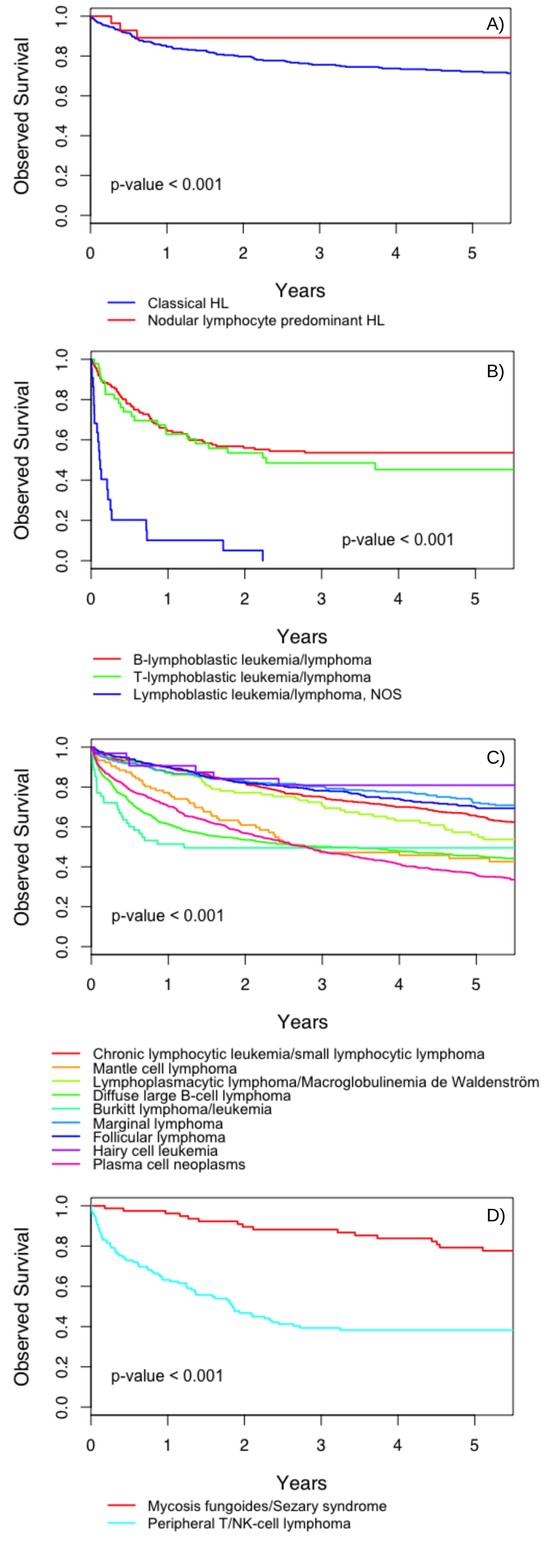

Figure 1. Observed survival of lymphoid neoplasms patients by subtype A) Hodgkin lymphoma, B) Precursor lymphoid neoplasms, C) Mature B-cell neoplasms and D) Mature-T-cell and NK-cell neoplasms. Girona province, 1996-2015.

CONCLUSIONS

- This is the first study to present epidemiological data from LNs in Spain according to the WHO 2008 classification.
- Marked variations by subtype and sex were demonstrated; confirming the importance of taking into account differences in lymphoid neoplasm subtypes when developing management strategies for these cancers and may also offer clues about their etiology.

References

1. Esteban L, Clèries R, Gálvez J, Pareja L, Escribà JM, Sanz X et al. REGSTATTOOLS: freeware statistical tools for the analysis of disease population databases used in health and social studies. Izquierdo A, Galcerán J, Ribes J. BMC Public Health. 2013 Mar 7; 13:201. doi: 10.1186/1471-2458-13-201.
2. Joinpoint Regression Program, Version 4.6.0.0 - April 2018; Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute.
3. Clèries R, Ameijide A, Buxó M, et al. [WebSurvCa: web-based estimation of death and survival probabilities in a cohort]. Gac Sanit. January 2018. doi:10.1016/j.gaceta.2017.10.015.

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